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HEMATOLOGICAL EFFECTS OF SPACE RADIATION*

by

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H.C. \$ 2.00; MN .50

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*Research supported by the U. S. Atomic Energy Commission.

Parts of this paper are being published in the monograph on Space Radiation Effects by the National Academy of Sciences Space Radiation Study Panel of the Life Sciences Committee of the Space Sciences Board. (Washington, D.C.)

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The hematological responses of man to short term exposure of "conventional" radiation are reasonably well known. Less is known about effects of protraction, fractionation, and quality of radiations to which man may be subjected in space. It is only natural that investigations in this direction have been very limited, not only because of the fact that interest in this problem has only recently become acute, but also due to the difficulties of research in problems associated with space. Useful data on the human being is extremely limited, and most of it that is at all helpful is derived from animal studies, most of which are not designed with space problems in mind. One is forced, therefore, to attempt some degree of extrapolation of animal data to man, which is, needless to say, fraught with uncertainty. Therefore, many questions can be only partly answered at this time.

In order to understand the hematological effects of irradiation to the space traveler, one must appreciate the special aspects of such an environment. Due to varying degrees of shielding afforded by the space craft, different parts of the blood-forming tissues of the astronaut will probably receive widely varying doses. The radiation intensity may vary considerably, and periods of high dose rates associated with solar flares will alternate with longer periods of lower dose rates or periods of negligible irradiation. He will be subjected to many different qualities of radiation with different depth-dose distributions within the body, and possibly with variable RBE for the blood-forming tissues. He will be subjected to various other stresses,

some of which may possibly augment the effects of ionizing radiation. In this chapter an attempt is made to evaluate these factors as they affect the degree of radiation damage to the blood-forming tissues and thereby the health and survival of the astronaut on which the success or failure of the mission may depend.

Hematological Responses to Short Term Irradiation

The hematological effects of exposure of animals and man to single doses of whole body radiation delivered over a short period of time (at dose rates $> 50-75$ rads/day) have been studied extensively. Observations of effects in man have been made on Japanese atomic bomb victims,^(1,2) the Marshallese natives exposed to fallout radiation,^(3,4) reactor and criticality accident cases,^(5,6,7-12) therapeutically irradiated cancer patients,⁽¹³⁾ and patients exposed for other medical reasons.⁽¹⁴⁻¹⁷⁾

Bone Marrow Damage. Hematological effects of radiation are dependent largely on damage to the critical organ system, the bone marrow. The blood-forming marrow is encased in bone, the amount of marrow varying from one bone to the other, the ribs, vertebral column, and pelvic bones containing the greatest amount. The role of the lymphatic tissues (outside the bone marrow), which furnish lymphocytes to the blood, is not well understood, but the lymphocyte is not considered as important to survival as are the other white cells. The degree of radiation damage to the bone marrow is reflected in peripheral blood counts. Lowering of levels of peripheral blood elements, therefore, is brought about largely by damage to the formative cells of the bone marrow and the cells of the lymphatic tissues. Inhibition of cell division and cytological damage in the bone marrow can be seen shortly after

irradiation. Heineke, as early as 1905, described destruction of bone marrow cells after irradiation,⁽¹⁸⁾ and since that time such changes have been well-documented.⁽¹⁹⁾ Fliedner, et al⁽²⁰⁾ have reported such findings in the Oak Ridge Y-12 criticality accident. Damage to the genetic apparatus of the cells, the chromosomes, was evident with inhibition of cell division (lowering of the mitotic index) and the presence of cells showing chromosome stickiness and bridges, fragmentation, etc. Chromosomal aberrations can also be detected in the cells of the peripheral blood by special techniques which will be referred to below. The degree of these bone marrow changes is dose-dependent and varies with time after exposure. As a rare late effect of radiation the marrow may become hypocellular or aplastic, or leukemia may develop. (See Chapter V.B.2.)

Blood Counts as an Index of Radiation Exposure. Since the degree of radiation damage to the bone marrow is reflected in the peripheral blood counts, radiation depression of blood-forming function has been studied largely via observations on the circulating blood rather than direct observations of the marrow. The time-course of changes in most of the peripheral blood elements is fairly well correlated with the dose of penetrating radiation. Based on dose relationship of these changes, four categories of prognostication in irradiated human beings may be made: survival almost certain (dose < 100 rads); survival probable (dose 100-200 rads); survival possible (dose 200-600 rads); survival improbable (dose > 600 rads). Figures 1-3 represent roughly the time-course of hematological elements in the human cases from accidental exposure for lymphocytes, neutrophils, and platelets in these four categories.⁽³⁻¹²⁾ The changes are represented in per cent of normal (per cent of the average levels for the population), and the curves portray generally the time-course of changes as a function of radiation dose.

The lymphocyte count (Fig. 1) is significantly depressed in 1-2 days, even with doses of less than 100 rads and approaches zero at that time with near-lethal doses. The return toward normal is slow and may be incomplete months and even years later, as has been the case with the exposed Marshallese people.⁽⁴⁾

Neutrophils increase in the first few days after exposure with doses greater than 100 rads (Fig. 2). This initial leukocytosis can be seen to be even greater with the higher doses. After this there is a steady decline with a leveling off or "abortive rise" between 8-20 days, except with lethal doses. Absence of this latter phenomenon following substantial radiation dose is a grave prognostic sign. Following the "abortive rise" further depression ensues, the nadir being reached earlier with higher doses; 8-10 days with lethal doses, to 40-45 days with sublethal doses. If profound neutropenia develops, serious or fatal febrile infections may develop. If the bone marrow is capable of sufficient regeneration before overwhelming infection and death occur, the neutrophil count will climb toward normal during the ensuing weeks, and recovery of the individual is likely. Complete return of counts to normal may be delayed for months, or with higher doses the levels may actually overshoot normal for a time.

Changes in platelet counts are shown in Figure 3. Lowest levels are reached about 24-32 days, except in lethal cases with survival improbable (> 600 rads) where levels may approach zero by 8-10 days. Bleeding is likely to develop when the platelets approach zero. With bone marrow regeneration, platelet recovery may begin rapidly but be incomplete for months or years.

FIGURE 1

FIGURE 2

FIGURE 3

Significant depression of red blood cells of anemia is usually not found following single doses of radiation unless the case is complicated by hemorrhage. It seems likely that symptoms due to depression of blood cell levels from injury to the blood forming tissues would be manifest in only a few individuals following a dose of 200 rads, but that a majority of people would show such symptoms following about 300 rads.

The inherent fluctuation in individual counts limits the usefulness of such hematological means as a direct biological dosimeter or precise detector of radiation damage. However, repeated hematological examinations afford valuable prognostic information. The lymphocyte count is valuable as an early criterion of radiation injury. If there are 1200 or more lymphocytes per cubic millimeter at 48 hours after exposure, it is unlikely that the individual has received a fatal dose. Lower lymphocyte counts at this time indicate more serious exposure. Neutrophil and platelet counts are of value in following the subsequent progress of irradiation exposure cases, as well as signifying in a general way the degree of seriousness of the exposure.

Chromosome Aberrations as an Index of Severity of Exposure. In recent years improved techniques for tissue cultures and chromosome preparations suitable for morphological studies^(21,22) have been developed. Such techniques have been used with in vitro and in vivo irradiation studies of the chromosomes of human somatic cells,⁽²³⁻²⁶⁾ mainly from peripheral blood cultures. Radiation-induced aberrations whose frequency is roughly dependent upon radiation dose have been demonstrated. The aberrations noted include variation in the number of chromosomes and morphological changes of the chromosomes or chromatids, such as breakage, deletions, exchanges, the appearance of ring and dicentric forms. Chromosome aberrations in short-term peripheral blood cultures of Y-12 Oak Ridge criticality cases were demonstrated by Bender and Gooch,^(27,28) the frequency of such aberrations may persist in the human being for years though declining in number.

Modifying Factors of Space Irradiation

As was pointed out earlier, irradiation of the blood-forming tissues in space will be influenced by a number of special aspects of exposure which are difficult to evaluate. These include: protraction and fractionation of radiation, non-uniformity of dose (partial body exposure, varying depth-dose patterns), quality of radiations (RBE), and influence of other stresses of space. Little is known about the hematological responses to protracted, fractionated, or partial body exposure in man to "conventional" radiation, and considerably less to responses associated with exposure to the wide energy spectrum of photon and particulate radiations likely to be encountered in space. Even less is known about the influence of other stresses of space flight or hematological responses. In spite of these difficulties, the hematological changes due to radiation exposure in space will probably be the best indication of the severity of radiation damage to the individual as a whole. Physical dosimetry will be a necessary adjunct to the interpretation of such data.

Protraction and Fractionation. It is well established that hematological changes associated with protracted or fractionated radiation will be less pronounced than from short term high intensity irradiation. This is due to recovery factors which come into play. With acute radiation a 10% non-recovery fraction has been postulated. With protracted radiation the recovery fraction is no doubt greater. Dye has estimated that an astronaut exposed to whole body dose of 1 rad per day or low-LET radiation for 45 days will accumulate an "equivalent residual dose of 25 roentgens."⁽²⁹⁾ Dose rate and quality of radiation will determine whether the complex destructive factors or regenerative factors will predominate for a given dose.

With protracted low dose rate radiation, such as may occur in radiation workers, observed hematological changes are slight, and the diversity of changes reported indicate their lack of clear-cut diagnostic value.⁽³⁰⁻³³⁾ Some of the changes reported include: increased white cell counts with relative increases of lymphocytes, decreased white cell counts (counts less than 5,000 over a period of time is a sign of overexposure), increase in size and number of red cells, and increased reticulocytes. Morphological changes include: the appearance of neutral red bodies in the cytoplasm of lymphocytes, the presence of bilobed lymphocytes, and the presence of multinucleated neutrophils.

Fractionated doses in animals show an increasing depopulation of cells in blood forming tissues with increasing dose rate.⁽³⁴⁻³⁶⁾ Based on peripheral blood counts the white cell series and platelets are more affected than the red cell series. It is interesting that in rats, in spite of continuous irradiation (100 rads/day of gamma), some degree of erythropoietic (but not myelocytic) regeneration occurs after 5 to 6 weeks exposure.⁽³⁷⁾

Protracted low dose x-irradiation (250-1000 Kvp) of dogs⁽³⁸⁾ showed a significant lowering of the mean level of peripheral blood elements as follows: lymphocytes by 2 years with 1 rad/day, neutrophils by 1 year with 1 rad/day, platelets by 1 year with 3 rads/day, erythrocytes by 1 year with 10 rads/day. Except for the 10 rads/day dose, few pathological findings could be related to radiation exposure in these dogs, in spite of the large accumulated doses. Doses of 10 rads/day, however, showed definite radiation related hematological effects, such as bone marrow and lymph node hypoplasia and hemorrhagic manifestations. Lamerton and Pontifex^(39,40) found in rats that 50 rads/day continuous x-irradiation over a period of 150-200 days was the highest dose at which maintenance of a steady state of peripheral blood counts was possible. If,

however, the daily dose rate were increased (30 rads/minute), lower daily doses were necessary to result in a steady state, and the peripheral blood counts were lower. In contrast with this, a steady state of regeneration of gut mucosa was possible with 400 rads/day. This implies greater regenerative capacity of the gut compared with bone marrow, at least in rats, and may possibly be explained by differences in regeneration and/or differences in feed-back mechanisms.

Due to the irreparable component of radiation injury, exposure to repeated doses in the human being will undoubtedly reduce the tolerance to subsequent doses. Experience with clinical radiotherapy indicates that patients receiving a second dose of whole-body radiation, even months after the first, show increased effects from the second dose. (13,41,42)

The Mexican accident⁽⁴³⁾ furnishes an example of the hematopoietic response of a family to protracted irradiation. The one survivor (the father in the family of five) was continuously exposed to an estimated daily dose of gamma radiation from Co⁶⁰ of 9.3 (maximum 16.2) rads for 106 days, giving a minimal total dose of 984 rads (maximum of 1,637 rads). His lowest recorded white count was 2,000 cells/mm³, and the lowest platelet count recorded was 70,000/mm³. The lowest counts were probably not sampled, but it is remarkable, assuming dosimetry was correct, that this large accumulated dose, even though spread over such a period of time, did not result in evidence of greater hemopoietic depression. The other members of the family received larger doses and undoubtedly died of complications of hemopoietic depression.

It is well known that low dose rates of x- and gamma radiation produce fewer chromosomal abnormalities than with high dose rates, while such dose rate effects are not noted with high LET radiation. (44)

Non-Uniformity of Dose. As pointed out, considerable variation of radiation doses to different parts of the bone marrow are likely to occur under space flight conditions due to variable shielding of the spacecraft and differences in energy and penetrability of radiations. Using the three solar flares of July 10-20, Dye⁽⁹⁾ has estimated that with shielding of 4 g/cm^2 an astronaut would have received 146 rads to the lens of the eyes, 43 rads to the sternal marrow, and 135 rads to the gut. In this case the sternal bone marrow would receive about 1/3 the dose to the lens; most of the remainder of the marrow would receive less.

Kaplan and Rosenberg have treated patients with Hodgkin's disease with 5 and 6 Mev x-irradiation using a sequential multiple port system.⁽⁴⁵⁾ Each field received several thousand rads over a period of about a month. Leukopenia (particularly lymphopenia) and platelet depression following a single port treatment seemed greater than would be expected on the basis of the percentage of marrow irradiated (abscopal effect?). However, in spite of the fact that during the 2-3 month period of treatment the majority of bone marrow had been irradiated with 2000-4000 rads, there were few complications of hematological depression. Important factors in this regard were probably the sequential nature of the partial body irradiation and the presence of unirradiated bone marrow.

Bond and Robinson⁽⁴⁶⁾ have developed a quantitative approach to evaluating the effects of non-uniform exposure and have pointed out that in non-uniform irradiation situations the unequal distribution of dose to the bone marrow would be expected to result in a greater survival rate than with the same average dose uniformly distributed because of the exponential nature of dose effect on survival of bone marrow stem cells. In addition, it is considered likely that

stem cells from unirradiated marrow may be transported to irradiated marrow to seed there and hasten regeneration.

Thus serious consideration should be given to shielding some of the bone marrow of the astronaut. The greatest benefit would probably accrue from local shielding of the pelvic region, since about 40% of the bone marrow of the body is located in this area.⁽⁴⁷⁾ Such a procedure would undoubtedly greatly increase the chances of survival in cases of serious irradiation. Also, the additional factor of shielding the genital organs would undoubtedly be of psychological benefit.

The radiation dose beyond which bone marrow regeneration cannot occur is not known for man but must be over 1000 rads. Kaplan noted recovery of sternal marrow in a patient that had received over 2000 rads. The critical dose of regeneration of the sternal bone marrow in mice has been found in the range of 2500-3000 rads of x-radiation delivered over a period of 2 to 4 weeks.

Quality of Radiation. The problem of hematological effects likely to be associated with various energy radiations, photon and particulate, encountered in space will be even more difficult to interpret as little data on such effects, even in animals, are available. Since these radiations will vary from radiations with energies that are relatively nonpenetrating to extremely high energy radiations, with wide variations of LET and RBE, it would appear that the blood forming tissues would receive a variety of possible REM doses. It is known that beta and alpha radiation of conventional isotopes will not penetrate the body sufficiently to produce any direct hematological effects, though secondary effects from irradiation of the skin may produce such changes as leukocytosis.⁽⁴⁸⁾ With somewhat more penetrating radiations

it is possible that lymphatic tissue might be more affected than bone marrow. In monkeys, irradiated with 32 MeV protons which penetrate to a maximum of 1 cm depth, depression of lymphocytes only was noted.⁽⁴⁹⁾ In this situation, without dosimetric assistance, the lymphocyte depression might be misleading as to the degree of generalized damage to the hematopoietic tissues.

Studies with small animals reveal that there are differences in RBE of various qualities of radiation which are both organ and species specific. For instance rodents, when compared with other species tend to have higher RBE values for fast neutrons.^(50,51) In this case the higher RBE is a reflection of greater sensitivity of both the gastrointestinal tract and bone marrow to these radiations. In the guinea pig fast neutrons were found to be twice as effective as 250 Kvp x-rays in producing death.⁽⁵²⁾ In this species the increased RBE for neutrons is related more to bone marrow injury, since gastrointestinal death does not occur in the lethal range. However, in larger animals such as the dog, bone marrow appears to have the same sensitivity to neutrons as to x-rays, though the gastrointestinal tract appears to be more sensitive to neutrons.⁽⁵³⁻⁵⁵⁾

The hematological responses to proton irradiation become very important in consideration of solar flare effects. Data are very limited on this subject. Dalrymple⁽⁴⁹⁾ and Lindsay and Dalrymple⁽⁵⁶⁾ have demonstrated in primates that the degree of hemopoietic injury is dependent on the penetrability (energy) of the protons. Such injury (as evidenced by depression of neutrophils, lymphocytes, platelets, and iron uptake) was not significantly greater in animals exposed to 250 and 400 Mev protons than with 2 Mev x-rays except that signs of hemorrhagic diathesis were greater. Such effects were less than x-ray effects when protons of 55 and 32 Mev energies were used, though relative lymphopenia was slightly

greater. Gastrointestinal effects were also more pronounced with higher energy protons. RBE for 30 day mortality, however, was about 1.

Taketa⁽⁵⁷⁾ reported that, using 730 Mev protons in monkeys, the RBE for hematological effects (depression of WBC) was about 0.7 using the midline tissue dose for comparison. (It should be pointed out that his LD₅₀ for Co⁶⁰ radiation was lower for his monkeys than reported by other investigators.)

Russian investigators⁽⁵⁸⁾ using protons of 126 and 510 Mev found an RBE of about 1 for hematological effects in dogs, though hemorrhagic manifestations were more severe, which they attributed to greater effects on the blood vessels. They found an RBE of < 1 for proton effects in rodents.

If the above findings in large animals hold true for man, then perhaps high energy particles of space radiation will produce about the same hematological effects as x- or gamma radiation.

Work is in progress by the Oak Ridge group to quantify the dose effect relationship for chromosome aberrations after exposure to various qualities of radiation. Studies on the RBE of various energy neutrons and protons indicate that the RBE was about 1 for energies above about 10-20 Mev, but that RBE increases with decreased energies below this range; neutrons in the fission energy range giving the highest RBE. Interpretation is complicated due to changing kinetics of the one-hit and two-hit aberrations with the increasing LET.

Other Factors. Other complicating factors in interpreting hematological response include the relatively unknown effects of other stresses of space flight, such as temperature extremes, barometric pressure effects, oxygen, and particularly weightlessness. Of importance are the recent

findings in astronauts of the Gemini V, VI, and VII flights of development of reduced plasma volume, reduced red cell mass, and shortened life span of red cells.⁽⁵⁹⁾ These changes were presumably induced by the weightless state, thus weightlessness might significantly aggravate radiation-induced hematological effects. There is some indication that the frequency of some types of chromosomal abnormalities is increased under weightless conditions from a preliminary study of blood cultures accompanying a Gemini mission. The increased frequency was believed due to impaired ability of the cells to repair chromosome damage.⁽⁶⁰⁾ Breathing of pure oxygen by the astronaut may enhance radiation effects.

Hematological Status and the Mission

Since the integrity of the blood forming tissues is of such importance to the success of the space mission, constant evaluation of blood changes is essential. In view of the known daily biological variation in blood counts and response to radiation exposure, it is essential that in-flight blood changes be evaluated in the light of (1) complete pre-flight baseline hematological data on each astronaut, (2) continuing dosimetric calculations, and (3) stresses other than irradiations.

Measurement of Blood Changes. For longer missions than Apollo, it is recommended that one of the occupants of the space vehicle be able to carry out simple blood counting from a drop of blood obtained by the finger-prick method on each occupant at intervals. Total white and differential counts yielding absolute lymphocyte and neutrophil counts would be sufficient. Equipment required for this would be minimal: a small microscope, counting

chambers, glass slides, and stain with staining jars. Special methods for working under weightless conditions would have to be developed. On return to earth, of course, further evaluation of radiation injury to the blood forming tissues by such examinations as platelet and reticulocyte counts, bone marrow study, cytogenetic studies, etc., would be carried out.

Hematological Indications for Abortion of Mission. In regard to blood levels necessitating the abortion of a mission, the decision will depend on a number of factors; such as, the accumulated dose of radiation, rapidity of blood changes, clinical signs and symptoms of radiation injury, effects of stress on blood counts, nearness to completion of mission, etc. However, generally speaking, if over 150 rads of whole body radiation in less than 48 hours are received, the white blood count drops to 2000 per cubic mm or below, or the neutrophil count drops below 1000 cells per cubic mm, or other signs of acute radiation sickness appear, serious consideration must be given to abortion of the mission.

Estimate of Dose Rate Effectiveness

It is believed that the general health and well being of the astronaut would be more seriously compromised by damage to the hematological system than to other organ systems. However, it is recognized that under certain circumstances the gastrointestinal and skin effects may seriously impair well being and performance ability but probably without as serious consequences. For example, if partial body shielding occurs, particularly if a pelvic shield is used, effects on other organs may predominate.

Marked variations in dose rates under space conditions are likely, varying from relatively fast dose rates associated with solar flares to slower dose rates of ambient cosmic and galactic radiation. The following scheme is designed to roughly estimate the effectiveness of various accumulated dosages to the astronaut based on dose rate relationship to hematological effects. Unfortunately, sufficient data is lacking to make such estimates with any degree of precision, and the scheme is only intended to serve as a crude guideline. Nevertheless, an attempted evaluation of dose rate effects is of importance in evaluating the overall effects on the astronaut.

For these purposes the following assumptions are made, recognizing that most of them are products of intuitive value judgements. (a) It is assumed that decreasing dose rates will be decreasingly effective on a linear basis. (b) That dose rates above 50 rads per day (considering dose rates likely to be encountered in space) will produce maximum effects. This dose rate has purposely been set conservatively low in view of the uncertainties of possible additive effects of other stress exposures in space. (c) Dose rates less than about two rads per day will produce minimal effects. (d) The maximum dose rate will be roughly three times as effective as the minimal in producing effects likely to reduce performance efficiency (effectiveness factor of 3).

From these assumptions, effectiveness factors for different dose rates may be applied to arrive at the effective dose (equal to the lowest dose rate effects). This is presented in the graph (Figure 4). The operating agency would set the allowable dosage for a particular mission, based on the lowest dose rate (less than 2 rads per day). The effective dose would be chronologically subtracted from this total allowable dose so that a continuing record is available for the remaining allowable exposure.

FIGURE 4
EFFECTIVENESS FACTOR

A hypothetical example is presented below of accumulated dosage of a space traveler, with the operating agency having set 450 rads as the allowable dose for a mission to last about a year.

<u>Date</u>	<u>Dose Rate (rads/day)</u>	<u>Dose</u>	<u>Effectiveness Factor</u>	<u>Effective Dose</u>	<u>Remaining Dose Allowed</u>
Jan. 1-24	< 2	5	1	5	450- 5=445
Jan. 24	>50	40	3	120	445-120=325
Jan. 25, 26	20-30	30	2	60	325- 60=265
Jan. 27-April 7	< 2	10	1	10	265- 10=255

It should be emphasized that this procedure serves only as a rough indication of dose rate effectiveness based on probabilistic terms for population, and it should be appreciated that due to unknown factors of population variance and other physiologic stresses the absolute response of an individual is not predictable. Therefore, the above values should be considered as an example of a working procedure for monitoring the accumulated dose of radiation and not as a recommendation of allowable dose.

It is important that in setting limiting doses of radiation for a mission operating agencies recognize fully the possible late effects of exposure such as leukemia, cataract formation, and life-shortening.

Need for Hematological Research

Atkinson,⁽⁴⁷⁾ in reviewing the distribution of active bone marrow in the human being as a function of age, points out the tenuous nature of the existing data. More recently Anger and Van Dyke⁽⁶¹⁾ have succeeded in more precise localization of functioning bone marrow using a positron scintillation camera. In view of the importance of the hematological effects of space radiation, more precise experimental data on the quantitative distribution of active bone marrow as a function of body region and age in the human being are

needed. Use of the Anger-type camera and positron emitters such as Fe^{52} or other isotopes such as $\text{Tc}^{199\text{M}}$ are helpful tools. Further information on the RBE for bone marrow for different quality radiations is indicated. More precise dosimetric evaluation of marrow effects will then be possible by collating the above data with distributional efficiency factors from various types of radiation, possibly using the model suggested by Bond and Robinson.⁽⁴⁶⁾

Since it is quite unlikely that research will be possible on healthy human beings, every effort should be made to exploit prospective and retrospective studies of hematological changes in patients undergoing radiation therapy and also in accident victims. Dose effect relationships of partial body and fractionated exposures with more accurate estimates of bone marrow dose would be extremely helpful.

Attempts to devise technical means of sampling and counting blood under weightless conditions should be looked into.

Much more information is needed on the combined effects of various environmental stresses of space with radiation stress on hematological response. This is particularly true in view of the recent observations on Gemini flights of the effects of weightlessness on the hematological system.

Summary and Conclusions

In summary, it would appear then from the data available, that the following conclusions might be drawn in regard to the hematological effects of space radiation on man.

(1) The bone marrow is, under most circumstances, the most critical organ for damage from radiation. The blood forming tissues possibly do not have the regenerative or renewal capacity that the gastrointestinal epithelium

has, and will, in most cases, be the limiting factor for survival. Neutrophil and platelet levels will be of primary importance in regard to the fitness and survival of the astronaut from the hematological point of view.

(2) Peripheral blood counts, both pre-flight and in-flight, for total white cell count (with neutrophil and lymphocyte levels) offer the best index of prognosis from the point of view of hematopoietic damage. Lymphopenia must be interpreted with caution, since dose distribution patterns and abscopal effects from partial body irradiation may give lower values than indicative of general bone marrow damage.

(3) The development of fever, infection, bleeding are signs of severe bone marrow damage.

(4) Abortion of a mission is indicated if an accumulated whole body dose of radiation of greater than 150 rads in a 48 hour period occurs; white blood counts drop below 2000 cells per cubic mm and neutrophils below 1000 cells per cubic mm; or if associated fever, infections, or bleeding occur.

(5) Very large doses of partial body radiation may be tolerated without lethal depression of circulating blood cells. Shielding part of the bone marrow may be an important factor in preventing serious hematological depression. It is recommended that serious consideration be given to providing shielding of part of the bone marrow of the astronaut. A lead apron over the pelvic region would shield about 40% of his bone marrow, and he could then withstand considerably larger doses of radiation to the remainder of his body.

(6) The dose rate and depth-dose distribution patterns of space radiation are the most important physical considerations in determining total bone marrow damage. High proton flux irradiation associated with solar flares presents the most serious radiation hazard.

(7) Based on limited data, the quality of radiation delivered to the bone marrow does not appear to present any special hazards, since the RBE appears to be about 1 or only slightly above for most space radiations that penetrate to the depth of the bone marrow.

(8) Indications for further hematological research are pointed out.

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